REMARKS

Status of the Claims

Claims 1-4, 6, 7, 9-15, 17, 18, 33-36, and 40-52 were pending in the present application.

Claims 1-4, 6, 7, 9-15, 17, 18, 33-36, and 40-52 were rejected.

Claims 7, 11, 18, 33, 40, 44 and 46-51 have been amended.

Upon entry of this amendment, claims 1-4, 6, 7, 9-15, 17, 18, 33-36, and 42-52 will be pending.

Summary of the Amendment

Claims 46 and 49 have been amended to recite the claimed invention more precisely. Support for the amendments may be found throughout the specification and claims.

Claims 7, 11, 18, 33, 44, 47, 48, 50 and 51 have been amended to recite "by intramuscular injection." Support for the amendment can be found on page 27, lines 13 – 15, of the specification.

Claim 40 has been amended to correct an obvious typographical error.

No new matter has been added.

Claim Objections

Claims 1-4, 6-7, 9-15, 17-18, 33-36 and 40-52 stand rejected as reciting non-elected subject matter. Applicants respectfully note that each of the claims read on the elected species. Upon concluding that the elected species is allowable, Applicants respectfully request that the generic claims which read on the elected species and a reasonable number of non-elected species be examined and allowed.

Claim Rejections Based Upon 35 U.S.C. §112, first paragraph

Claims 1-4, 6-7, 9-15, 17-18, 33-36, and 40-45 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing the enablement requirement. The Office asserts that it would have required undue experimentation to practice the scope of the invention as claimed. Applicants traverse the rejection and respectfully request that the rejection be withdrawn.

The Official indicates that

> the specification, while being enabling for 1) a method of immunizing a mammal against influenza comprising co-administering a plasmid DNA encoding Influenza HA and a plasmid encoding DR5 by intramuscular injection and 2) a pharmaceutical composition comprising a plasmid encoding Influenza HA and a plasmid encoding DR5 by intramuscular injection does not reasonably provide enablement for pharmaceutical composition comprising a plasmid encoding Influenza HA and a plasmid encoding DR5 or for methods of enhancing an immune response or methods of immunizing against any pathogen by administering plasmid(s) encoding an immunogen and DR5.

Claims 47 and 50 have been amended to recite that the methods of immunizing against influenza comprise intramuscular injection, thereby referring to methods of immunizing a mammal against influenza comprising co-administering plasmid DNA encoding Influenza HA and DR5 by intramuscular injection.

The Official Action also indicates that

> while claims 7, 18 and 33 have been amended to recite methods of inducing a CTL response, the recited methods continue to broadly encompass any route of administration, and claim 33 further continues to broadly claim the administration of any nucleic acid molecule rather than a plasmid or plasmid(s).

Claims 7, 18 and 33 have been amended to recite that the methods comprise intramuscular injection. Claim 33 continues to recite nucleic acid molecules generically because Applicants respectfully urge that, in view of all of the evidence of record, those skilled in the art would

accept Applicants' assertion of enablement for the subject matter of claim 33, as well as the subject matter in claims 34-36, 45 and 53 which are each dependent on claim 33.

Applicants respectfully urge that claims 1-4, 6, 9, 10, 12-15, 17, and 40-43, which recite various compositions and pharmaceutical compositions useful in the methods of one or more of claims 7, 18 and 33, are enabled by the specification and the declaration. The evidence of records, when viewed in its totality, supports the finding of enablement of these claims.

Claims 11, 44, 48 and 51, which refer to methods of immunizing, have each been amended to refer to intramuscular injection. Applications respectfully urge that in view of the totality of evidence on the record, one skilled in the art would accept Applicants' assertion that the claims are enabled.

One skilled in the art would accept the enablement of claimed invention. The evidence of record adequately supports the conclusion that one of ordinary skill in the art could practice the claimed invention without undue experimentation. Applicants respectfully request that the rejection of claims based upon 35 U.S.C. §112, first paragraph, be withdrawn.

Claim Rejections Based Upon 35 U.S.C. §102

Claims 1–3, 6, and 12 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent number 6,417,328 (hereinafter "Alnemri"). Applicants respectfully disagree and respectfully request that the rejection based upon 35 U.S.C. § 102(e) be withdrawn.

It is well established that, in order to anticipate the claims, a prior art reference must explicitly or inherently disclose each and every element of the claims either. Applicants maintain that Alnemri does not teach or disclose every element of the rejected claims. The claims recite a pyrogen-free composition comprising a plasmid that comprises a nucleic acid sequence that encodes an immunogen and an immunomodulating protein (claims 1-3 and 6) and a pyrogen-free composition comprising a plasmid that comprises a nucleic acid sequence that encodes an immunogen and a plasmid that comprises a nucleic acid sequence that encodes an immunomodulating protein (claim 12). Nowhere in Alnemri do authors teach or remotely

suggest combining a nucleic acid sequence that encodes an immunomodulating protein such as DR5 with a nucleic acid sequence that encodes an immunogen in a pyrogen-free composition.

The Office has improperly characterized the teachings in Alnemri to support its position that Alnemri anticipates the claims. Specifically, the Office has pointed to and combined two sections of Alnemri which were clearly directed at different concepts. One section of Alnemri, Example IV which discloses a plasmid encoding DR5 is used in an apoptosis function assay that employs lacZ coding sequences as a detectable expression marker. Another section of Alnemri refers to the use of a plasmid encoding DR5 as a therapeutic. The Office asserts that the section referring to therapeutics would include the constructs used in the apoptosis assay. That is not what Alnemri teaches and one skilled in the art would not conclude that Alnemri intended such an interpretation. There is no disclosure of using lacZ encoding constructs in the therapeutics disclosed in Alnemri and no reason is provided why such an interpretation could properly be supported. The position offered by the Office is not reasonable. One skilled in the art would not read Alnemri and conclude that the constructs used in the assays described in the Examples would be employed in the therapeutic compositions also described in the specification.

Alnemri does not disclose the subject matter set forth in the claims. In view of the foregoing, Applicants respectfully request that the rejections of claims 1 - 3, 6, and 12 under 35 U.S.C. § 102(e) as being anticipated by Alnemri be withdrawn.

Claim Rejections Based Upon 35 U.S.C. §103

Claims 1–3, 6, and 12 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Alnemri in view of US Pat. No. 5,693,622 (hereinafter "Wolff"). Applicants respectfully disagree and traverse the rejection.

Alnemri is discussed above.

Wolff is cited as teaching purification of plasmids using cesium chloride gradients.

It is asserted that it would have been *prima facie* obvious to one skilled in the art to purify the constructs disclosed in Alnemri using the purification techniques disclosed in Wolff to produce constructs for use *in vivo*. Applicants respectfully disagree.

There is no motivation to combine the references and so a *prima facie* case has not been made. The immune enhancing activity of Dr5 is unexpected and, accordingly, one skilled in the art would not be motivated to produce an injectable composition that comprises coding sequences of DR5 with an immunogen.

Nothing in Alnemri teaches or suggests why one skilled in the art would employ the purification techniques disclosed in Wolff to purify the constructs used in the *in vitro* assay in Example IV. The marker sequences were included in the constructs for detection in the *in vitro* assay. There is no suggestion why one skilled in the art would employ such constructs in an *in vivo* application. One skilled in the art would not be motivated to combine the teachings of Alnemri of constructs encoding Dr5 and the disclosed expression markers with the teachings in Wolff in the absence of such motivation, there is no *prima facie* case of obviousness. there is no motivation to produce the claimed compositions.

There is no motivation to combine references. One skilled in the art would not expect that a pyrogen free composition encoding Dr5 and an immunogen protein would produce an enhanced immune response. One skilled in the art would not expect that Dr5 would have immune enhancing properties. Thus, One skilled in the art would not produce an injectable composition that would include coding sequences for Dr5 in combination with coding sequences for an immunogen.

Applicants contend that the invention was not *prima facie* obvious at the time of the invention. In establishing a *prima facie* case of obviousness under 35 U.S.C. § 103, it is incumbent upon the Office to provide a reason why one of ordinary skill in the art would have been led to modify a prior art reference or to combine reference teachings to arrive at the claimed invention. Ex parte *Clapp*, 227 U.S.P.Q. 972 (Bd. Pat. App. Int. 1985). To this end, the requisite motivation must stem from some teaching, suggestion or inference in the prior art as a whole or

from the knowledge generally available to one of ordinary skill in the art and not from appellants' disclosure, see for example, *Uniroyal Inc. v. Rudkin-Wily Corp.*, 5 U.S.P.Q.2d 1434 (Fed. Cir. 1988); and Ex parte *Nesbit*, 25 U.S.P.Q.2d 1817, 1819 (Bd. Pat. App. Int. 1992). In this respect, the following quotation from Ex parte *Levengood*, 28 U.S.P.Q.2d 1300, 1302 (Pat. Off. Bd. app. 1993), is noteworthy:

> Our reviewing courts have often advised the Patent and Trademark Office that it can satisfy the burden of establishing a prima facie case of obviousness only by showing some objective teaching in either the prior art, or knowledge generally available to one of ordinary skill in the art, that "would lead" that individual "to combine the relevant teachings of the references." … Accordingly, an examiner cannot establish obviousness by locating references which describe various aspects of a patent applicant's invention without also providing evidence of the motivating force that would impel one skilled in the art to do what the patent applicant has done. (citations omitted)

The Office Action identifies no "motivating force" that would "impel" persons of ordinary skill to modify or combine the respective teachings of the cited references and achieve the claimed invention. Neither Alnemri nor Wolff teach, disclose, or suggest a composition comprising a nucleic acid molecule that encodes an immunogen and a nucleic acid that encodes an immunomodulating protein. Neither Alnemri nor Wolff teach, disclose, or suggest that DR5 could be used as an immunomodulating protein. No one of ordinary skill in the art would think to modify the references to generate a composition useful to enhance an immune response generated against an antigen. One of skilled in the art would have to use hindsight to take the plasmid of encoding lacZ and DR5 and, replace the lacZ gene with an immunogen, and create a composition useful to enhance the immune response. Such a modification of Alnemri would be completely illogical based upon what was known at the time of filing the application for the current invention. As such, the *prima facie* case of obviousness is not established by Examiner.

Applicants respectfully request that the rejection based upon 35 U.S.C. § 103(a) be withdrawn.

Conclusion

Claims 1-4, 6, 7, 9-15, 17, 18, 33-36, and 42-52 are in condition for allowance. A notice of allowance is earnestly solicited.

The Commissioner is hereby authorized to charge any deficiencies of fees and credit of any overpayments to Deposit Account No. 50-0436.

Respectfully submitted,

/Mark DeLuca, Reg. No. 33,229/
Mark DeLuca
Registration No. 33,229

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PEPPER HAMILTON, LLP
400 Berwyn Park
899 Cassatt Road
Berwyn, PA 19312-1183
Telephone: 610-640-7855
Facsimile: 610-640-7835